condition for consideration on appeal, does not present additional claims, new matter, or issues requiring further consideration or search.

1. THE APPLICATION MEETS THE UTILITY REQUIREMENT OF 35 U.S.C. § 101

Pending claims 1-3 were rejected under 35 U.S.C. § 101 because the claimed invention was allegedly not supported by either a "specific asserted utility" or a "well-established utility". The Examiner stated:

> the only apparent *immediate* utility for the EST, and therefore the claimed nucleic acid molecules, is further characterization of the EST, which includes characterization of undisclosed products made from or with the claimed nucleic acid molecules. Such *immediate* utility constitutes use testing. There is no "*immediate* benefit to the public."

Office Action dated March 22, 2000 at page 16, *citing Brenner v. Manson*, 383 U.S. 519, 534-35, 148 U.S.P.Q. 689, 696 (1966). The Examiner also stated that "the application fails to disclose practical, real world utilities for the claimed nucleic acids comprising or consisting essentially of SEQ ID NO:1." Office Action dated March 22, 2000 at page 17.

This analysis misstates the nature of the asserted uses, ignores disclosed utilities, and misapplies the doctrine of "practical utility" developed by the courts after *Brenner v. Manson*. It is well-established law that "when a properly claimed invention meets at least one stated objective, utility under section 101 is clearly shown." *Raytheon Co. v. Roper Corp.*, 724 F.2d 951, 958, 220 U.S.P.Q. 592, 598 (Fed. Cir. 1983). Applicants respectfully traverse the rejection, because the claimed nucleic acid molecules are supported by specific, well-established "real world" utilities as described in the specification and as proven by experimentation. Although Applicants only need to establish a single utility to satisfy 35 U.S.C. § 101, all of the issues raised by the Examiner are addressed herein.

a. The Claimed Nucleic Acid Molecules Have Utility

The Examiner asserts that the claimed nucleic acid molecules lack utility for three reasons: first, the correspondence of an isolated cDNA to a functional mRNA *in vivo* is merely

illusory; second, that an isolated cDNA is an artifact; and third, that the claimed nucleic acid molecules have no "real world" value.

a.1. ESTs and nucleic acid molecules with EST sequences have utility as they correspond to *in vivo* nucleic acid molecules

Nucleic acid molecules with EST sequences are fundamentally different from non-biological chemicals that have been the subject of prior decisions under 35 U.S.C. § 101, because the EST sequence is a sequence of part of an mRNA molecule that performs a real function in nature. This is an inherent quality of nucleic acid molecules, which are partial sequences of cDNA clones. A cDNA, by definition, has a complementary base sequence to an mRNA molecule. Therefore, an EST sequence corresponds.

The Examiner questions that correspondence, asserting that "it is not true that an EST definitely corresponds to a functional gene or gene product ... because the EST may correspond to a pseudogene" and "as such the asserted basis for utility that an EST relates to an mRNA functional *in vivo* is illusory". Office Action dated March 22, 2000 at page 6. As purported support for this premise, the Examiner cites to Brandt *et al., Curr. Genet. 24.4:* 330-336 (1993); Quinones *et al., Plant Mol. Biol. 31.4:* 937-943 (1996); Mundel *et al., Curr. Genet. 30.5:* 455-460 (1996) and Barakate *et al., Mol. Biol. 229.3:*797-801 (1993)). The Examiner's reliance on these references is misplaced because it fails to appreciate that the transcripts of mitochondrial mRNA pseudogenes lack the poly A tails which nuclear mRNAs have.

The first three of the foregoing references report ***mitochondrial*** transcribed pseudogenes. Significantly, no nuclear transcribed pseudogenes were reported. Therefore, the references do not suggest that the claimed nucleic acid molecules would correspond to any pseudogenes. A cDNA library (such as the one disclosed in the present Application) generated using an oligo d(T) primed reverse transcriptase reaction will not normally contain copies of mRNA derived

from ***mitochondrial*** DNA. Declaration of Roger C. Wiegand, Ph.D. (hereinafter "Wiegand Decl.") at 5.[1]

Indeed, such cDNA libraries are often generated using primers that bind to the poly A tails of nuclear mRNAs. Clonetech's SMART cDNA kits use such primers (Clonetech, Palo Alto, California). Unlike nuclear mRNAs, ***mitochondrial*** mRNAs lack the poly A tail. Accordingly, cDNA libraries, such as the one disclosed in the present application, which are generated using an oligo d(T) primed reverse transcriptase reaction, will not normally include copies of mRNAs derived from ***mitochondrial*** DNA. As a result Brandt *et al.*, Quinones *et al.*, and Mundel *et al.* do not support the Examiner's proposition of illusory correspondence between a functional mRNA and the claimed nucleic acid molecules.

Furthermore, Barakate *et al.* does not, as the Examiner contends, disclose the "phenomenon of transcribed pseudogenes." Office Action dated March 22, 2000 at page 6. At page 801, Barakate *et al.*, report "[w]e asked whether the exoPG pseudogenes were transcribed. No transcript corresponding to the size of the exoPG pseudogenes was detected." Barakate *et al.*, like Brandt *et al.*, Quinones *et al.*, and Mundel *et al.*, fail to support in any way whatsoever the Examiner's assertion that the correspondence between a functional mRNA and a cDNA is illusory. In essence, the Examiner's contention that the claimed nucleic acid molecules may correspond to a pseudogene is speculation not backed up by any of the cited documents. The Office's burden is to provide evidence to support a rejection, not just speculation.

a.2. The Claimed Nucleic Acid Molecules Correspond to Functional *in vivo* Molecules

The Examiner states that "it is more likely than not that the EST disclosed as SEQ ID No: 1 is an artifact that does not correspond sufficiently to a naturally occurring soybean nucleic

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[1] While the existence of cDNA clones that correspond to a mitochondrial mRNA in a library cannot be completely eliminated, such cDNA clones are rare. Such rare possibilities cannot support speculation that the claimed nucleic acid molecules corresponds to a mitochondrial mRNA and not a nuclear mRNA that performs a function *in vivo*. Moreover, SEQ ID No. 1 is not similar to any known mitochondrial sequence. Wiegand Decl. at para. 5.

acid". Office Action dated March 22, 2000 at page 6. This is clearly not the case. Applicants have demonstrated that a nucleic acid molecule having SEQ ID No: 1 was synthesized and that it hybridized to a naturally occurring nucleic acid molecule in soybean. Wiegand Decl. at paras. 16-19.

The issue is not whether the claimed nucleic acid molecules exhibit 100% correspondence with a naturally occurring soybean nucleic acid. It is not necessary, nor has the Examiner shown that it is necessary, that the claimed nucleic acid molecules exhibit 100% correspondence with a naturally occurring soybean nucleic acid to "work". The Examiner is reminded that utilities asserted in the specification must be accepted as factually sound unless the Patent Office cites information that undermines the credibility of the assertion. *In re Brana,* 51 F.3d 1560, 1566, 34 U.S.P.Q.2d 1436, 1441 (Fed. Cir. 1995). In the Office Action, the Examiner provides no evidence challenging whether the claimed nucleic acid molecules would work for the disclosed utilities. That the claimed nucleic acid molecules can work without 100% correspondence with a naturally occurring molecule is clear. To practice many of the disclosed utilities all that is necessary is for the claimed nucleic acid molecules to hybridize to a naturally occurring molecule.

Furthermore, notwithstanding the Examiner's purported technical problems regarding the correspondence between the nucleic acid molecule and a naturally occurring soybean nucleic acid, such nucleic acid molecules with EST sequences are routinely used, for example, to detect expression levels of corresponding naturally occurring soybean nucleic acids. Wiegand Decl. at para. 14. The fact that such molecules "work" (and work routinely) for that intended purpose is alone sufficient to establish that the claimed nucleic acid molecules possess requisite legal utility.

Nevertheless, to support his assertion that the EST is an artifact, the Examiner points to a number of purported technical problems that would in the Examiner's view result in the EST corresponding to an artifact. Quite apart from whether those purported problems are relevant or

even real, they do not individually or together lend support to the erroneous conclusion that the EST is an artifact that would not work for the disclosed utilities.

First, the Examiner suggests that the process of polymerase chain reaction (PCR) is error prone and that a significant fraction of the final nucleic acid molecules contain misincorporated nucleotides. Office Action dated March 22, 2000 at page 4. But the Examiner has failed to show or even argue that because PCR misincorporates nucleotides, molecules containing "misincorporated" nucleotides will not work for disclosed utilities. Indeed, the contrary is true. As set forth in the accompanying Declaration, notwithstanding the issue of misincorporation of nucleotides, PCR-generated nucleic acid molecules are routinely and effectively used in the industry. Wiegand Decl. at para. 8.

Second, the Examiner states "it is more likely than not that the disclosed EST, SEQ ID No: 1, is derived from a repeated sequence, and there is a significant chance that it is a chimera of related sequences." Office Action dated March 22, 2000 at page 5 (emphasis added). Again the Examiner has failed to show or even argue that even if this statement is true, the resulting nucleic acid sequence will not have the disclosed utilities. But equally important is the fact that chimeric and repeated cDNAs are significantly rarer than the Examiner suggests (*see* Wiegand Decl. at para. 8), and the speculation that they might exist with the disclosed EST does not provide a reasonable basis upon which a utility rejection can be made.

In sum, it is not Applicants' burden to prove a negative, rather it is the Examiner's burden (not met here) to establish a reasonable basis to assert that the claimed nucleic acid molecules are probable artifacts, not merely that there is some probability that they might be. In any event, the Declaration of Dr. Wiegand at paragraphs 18 and 19 shows that the claimed nucleic molecules will hybridize to a naturally occurring soybean nucleic acid molecule, proving that the ESTs are not artifacts.

a.3. ESTs and nucleic acid molecules with EST sequences have commercial value

The utility requirement of Section 101 is merely a shorthand of attributing "real-world" value to claimed subject matter. *Nelson v. Bowler & Crossley,* 626 F.2d 853, 856, 206 U.S.P.Q. 881, 883 (C.C.P.A. 1980). Contending that ESTs and nucleic acid molecules with EST sequences lack "real world" value that establishes "utility" in its patent law sense, ignores industries that the patent system was created to serve and to foster. As noted in Applicants' Response dated July 6, 1999, the "utility" of ESTs is not merely an academic issue; the "real-world" value of ESTs is self-evident from the growth of a multi-million dollar industry in the United States premised on the usefulness of ESTs. *See* Wiegand Decl. at para. 6.

Furthermore, the Examiner misapprehends the commercial value of ESTs. The Examiner asserts that while EST databases are capable of generating revenue, the instant claims are drawn to nucleic acid molecules, not EST databases, which are collections of information. Moreover the Examiner asserts that such commercial success is not dispositive because commercial success is impacted by a variety of factors such as advertising and marketing. Office Action dated March 22, 2000 at page 7.

But the Examiner fails to credit why EST databases are capable of generating revenue. Willingness to buy such access is based on the underlying biological value of the nucleic acid molecules, not the mere strings of nucleotides in the database. In other words, it is the biological attributes of the nucleic acid molecules with EST sequences that are the basis for the value associated with the referenced deals. "EST agreements" often require the transfer of either the clones from which the ESTs were obtained or the information necessary to make nucleic acid molecules with EST sequences. Wiegand Decl. at para. 6. And even where clones are not transferred, the database access merely assists in the selection of appropriate clones to pursue and allows comparisons between the sequences in the database and other sequences, either in the database or available elsewhere. The Examiner is clearly in error when failing to credit the value

of the underlying sequenced clones, *i.e.*, the nucleic acid molecules. Indeed, he wrongly asserts that the molecules themselves have no value in the multi-million dollar industry which has developed.

The Examiner also provides no basis for the suggestion that commercial success of that industry is so impacted by additional factors such as advertising or marketing as to render any value resulting from the molecules trivial. No correlation or suggestion of advertising or marketing impact has been provided. Indeed such an assertion flies in the face of commercial reality when many of the agreements referred to in the submitted articles reference transactions between corporations that were the result of arms length negotiations. Furthermore, the market participants for EST products are primarily sophisticated corporations and highly knowledgeable scientists who are unlikely to make commercial and scientific decisions regarding the value of ESTs based on how the ESTs are advertised.

b. Tools have legal utility

The Examiner has argued that several of the asserted utilities are directed to use of the claimed nucleic acid molecules as tools, *e.g.*, hybridization probes, and that such utilities lack legal significance. This is wrong as a matter of law. The fact that, for example a new and nonobvious microscope or cell based drug screening technology can be used for learning about products or processes does not lessen the fact that such "tools" have legal utility. One legal utility of a microscope is its use to look at the structure of biological tissues placed under the microscope (electron microscopes can, of course, be utilized to look at intracellular structures). Many of the utilities that are disclosed in the specification are directly analogous to the utilities of a microscope, *i.e.*, the claimed nucleic acid molecules may be used to locate and measure nucleic acid molecules within a sample, cell or organism. This use is not legally different from the legally sufficient use of a microscope to study structure.

Cell-based assays have been developed that allow the practitioner to screen compounds for a certain attribute such as the ability to bind a cell receptor involved with a biological process. Such cell-based assays can be used to screen for desired compounds. Many of the utilities disclosed in the specification are directly analogous to such screening assays, *e.g.*, the claimed nucleic acid molecules can be used to screen for polymorphisms. Such uses are legally sufficient to establish utility.

c. The Present Application Discloses Specific Uses of the Claimed Nucleic Acid Molecules

Even if the biological function were not sufficient for purposes of statutory utility, the other disclosed utilities are themselves sufficient.

The Examiner states that "[g]eneralized utilities lack the specific correspondence between the asserted utility and the claimed subject matter required by the statute" Office Action dated March 22, 2000 at page 8. The Examiner apparently asserts that such specific correspondence is lacking because the only characteristic provided by Applicants is a single nucleotide sequence and that "one cannot determine from the disclosed nucleotide sequence alone [other characteristics like] corresponding map location; presence or absence of physically-linked polymorphisms ... identity of any specific plant tissue expressing the corresponding mRNA ... or the identity of naturally occurring mutations ... ." Office Action dated March 22, 2000 at page 8. Applicants note that the Examiner's assertion is clearly inaccurate because Applicants provide more than a single nucleotide sequence, for example, the specification discloses the identity of a specific plant tissue expressing the corresponding mRNA.[2] But even if the quoted passage were true, the claimed nucleic acid molecules can, without undue experimentation,[3] be used to

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2 The specification discloses the identity of the specific plant tissue expressing the mRNA corresponding to SEQ ID No.: 1, namely young seed pods, at page 67, Example 1.

3 *See* Section 2, *infra*.

determine such useful attributes as the presence or absence of polymorphisms and the "corresponding map position" of the claimed nucleic acid molecules.

c.1. Identifying the presence or absence of a polymorphism

One can use the claimed nucleic acid molecules to identify the presence or absence of a polymorphism, which is one of the disclosed utilities. The Examiner asserts that without the prior identification of a polymorphism, such use is legally insufficient "use testing." Office Action dated March 22, 2000 at pages 9-10. That assertion is wrong because using the claimed nucleic acid molecules to screen for polymorphisms is no more legally insufficient than using a biological assay to screen for chemicals which themselves might not have legal utility. The assay and biological constituents of such an assay nevertheless have legal utility. Likewise the claimed nucleic acid molecules have legal utility even if the polymorphism itself lacks legal utility.

Furthermore, the Examiner provides no support (legal or factual) for the proposition that before detection of polymorphisms could be recognized as a legal utility, actual polymorphisms must be shown to exist. The fallacy in the Examiner's position is especially the case when (as here) the Examiner provides no evidence suggesting that the claimed nucleic acid molecules would be unable to identify a polymorphism, if one is present. In any event, the issue is whether the claimed nucleic acid molecules could be used to screen for the presence or absence of polymorphisms. The latter can be accomplished even when no polymorphism is detected in a screened population.

Moreover, and notwithstanding the fact that a *prima facie* case for a utility rejection has not yet been made, Applicants refer to the accompanying Declaration, which reports that a nucleic acid molecule having the sequence of SEQ ID No: 1 does detect polymorphisms in a population of plants derived from a cross between the soy varieties *Glycine max* and *Glycine soja*. Wiegand Decl. at paras. 22-23. The Declaration also confirms that nucleic acid molecules capable of detecting polymorphisms are useful in plant breeding. *Id.* at paras. 20, 23.

c.2. Use of the claimed nucleic acid molecules for determining location on a physical map or genetic map and for screening

A second utility for the claimed nucleic acid molecules is to use the claimed nucleic acid molecules for determining location on a physical map or genetic map location, *i.e.*, to use the claimed nucleic acid molecules as molecular markers. The Examiner asserts that the application provides no information on either the physical or genetic map location or a polymorphism by which the genetic position could be determined. Office Action dated March 22, 2000 at page 10.

The Examiner is wrong in asserting that prior to using the claimed nucleic acid molecules to determine location on a physical map or genetic map location, the copy number[4] of the sequence would have to be determined. Office Action dated March 22, 2000 at page 11. The claimed nucleic acid molecules can, without more, be used to determine a physical or genetic map location. Thus, without knowing anything beyond the sequence of the claimed invention, one can use the claimed invention. *See* Wiegand Decl. at para. 12. Nevertheless, the Examiner also asserts that utility for mapping the chromosomal position of a marker (*i.e.*, the claimed molecule) is not legally sufficient because knowing its location "is at best a scientific curiosity." Office Action dated March 22, 2000 at page 12. This is also wrong. The development of molecular markers is a practical activity in the development of nutritionally enhanced or agriculturally enhanced crops, not a mere scientific curiosity. Such markers are useful in, for example, genetic mapping or linkage analysis, marker-assisted breeding, physical genome mapping, transgenic crop production, crop monitoring diagnostics, and gene identification and isolation. As more markers are identified, genetic maps will become more detailed and it will be easier for plant breeders to breed for particular traits. Copies of articles discussing a number of

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4 As used by the Examiner, copy number refers to the number of times a particular nucleic acid sequence occurs in a genome.

commercial efforts directed to the generation of such plant molecular markers are enclosed for the Examiner's reference.[5]

c.3. Use of the claimed nucleic acid molecules to measure the level of an mRNA in a sample

The claimed nucleic acid molecules can be used to measure the level of an mRNA in a sample. The Examiner asserts that absent any phenotypic consequences associated with expression no significant information can be gleaned and its utility is therefore unclear.

It is standard practice to screen populations of nucleic acids representing ESTs, often attached to a microarray, with various biological samples to study the expression of the corresponding genes. Knowing that the gene corresponding to the claimed nucleic acid molecules is expressed under certain conditions or in certain tissues or at certain levels *etc.* is in itself useful. *See* Wiegand Decl. at para. 14. For example, such information is useful to detect expression changes in traits of interest, *e.g.*, drought stress. As such, the claimed nucleic acid molecules are important components of such an assay by providing additional data points, and it is their importance as components of the screening assay that provides patentable utility.

Thus, the Examiner is in error in stating that "[one] would first be required to determine the ... characteristics in order to then begin the process of determining a use." Office Action dated March 22, 2000 at page 15. Indeed determining such characteristics is an important use.

c.4. Use of the claimed nucleic acid molecules as a probe for other molecules or as source for primers

The Examiner asserts that the claimed nucleic acid molecules lack utility as probes for other molecules or as a source for primers because the specification has not disclosed any

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[5] The Examiner thus wrongly suggests that use of the claimed nucleic acid molecules as a chromosome marker or in one of the other disclosed uses is insubstantial because it lacks real world value. (Office Action dated March 22, 2000 at page 16). In any event, using the claimed nucleic acid molecules for not only mapping the location of the corresponding gene but also to screen for desirable traits is not, as suggested by the Examiner, use testing, but is the use of the claimed product to perform a valuable real world activity as evidenced by these accompanying articles.

specific nucleic acid molecule that can be identified using the claimed nucleic acid molecules. This is not correct.

The Application has disclosed, for example, that the claimed nucleic acid molecules can be used to isolate nucleic acid molecules of other plants and organisms such as alfalfa, rice, potato, cotton, oat, rye, barley, maize, wheat, *Arabidopsis, Brassica, etc.* Specification at page 24, lines 13-26. No evidence or suggestion has been provided that this cannot be done.

One illustrative example of a molecule that can be isolated using the claimed nucleic acid molecules is the promoter of the gene corresponding to the claimed nucleic acid molecules. Applicants have specifically disclosed that one use of the claimed nucleic acid molecules is to initiate a chromosome walk. Specification at page 25, lines 26-27. The Examiner, however, seems to denigrate that utility when he asserts that the claimed nucleic acid molecules, "at best ... can be used to initiate a 'chromosome walk' cloning procedure" and that "[a]ny nucleic acid molecule from any plant cell generally serves this purpose ... ". Office Action dated March 22, 2000 at page 13. In short, the Examiner suggests that the utility is not a legal utility simply because other molecules can be used for the same purpose. That position is wrong as a matter of law – there is no requirement of exclusive utility in the patent law. *See Carl Zeiss Stiftung v. Renishaw PLC*, 945 F2d 1173, 1180, 20 U.S.P.Q.2d 1094, 1100 (Fed. Cir. 1991) ("An invention need not be the best or the only way to accomplish a certain result...").

Moreover, Applicants do not agree that the claimed nucleic acid molecules merely provide an equally good starting point for such a walk. Indeed, the claimed nucleic acid molecules provide an appropriate and useful starting point for a walk to isolate a promoter that is active in young pods (5 to 15 days after flowering). Such a promoter would, for example, be particularly useful in expressing proteins at that important development stage. Such proteins could, for example, include proteins that provide disease resistance. A random nucleic acid molecule does not provide an equally good starting point to isolate such a promoter.

In further challenging the utility, the Examiner asserts that the "chromosome walk" might be quite long. But the question is not whether the claimed nucleic acid molecules would necessitate a long "walk" but whether the claimed nucleic acid molecules will work for the disclosed use. The Examiner has failed to provide any evidence or suggest that the claimed nucleic acid molecules could not be so used. Accordingly the assertion of this utility satisfies the requirements of 35 U.S.C. §101. *See In re Brana*, 51 F.3d 1560, 1566, 34 U.S.P.Q.2d 1436, 1441 (Fed. Cir. 1995).

Perhaps in recognition of the foregoing inadequacies in the rejection, the Examiner also asserts that Applicants provide no information that would allow those of ordinary skill in the art to recognize when a promoter is located. But that assertion is incorrect, as Applicants have directed the art worker toward Birren *et al., Genome Analysis: Analyzing DNA,* Cold Spring Harbor, New York, NY (1997), which provides such information. Specification at page 26, lines 12-15. For example, the nucleotide sequence of a region suspected to contain a promoter sequence can be compared to known promoter motifs and sequences.

c.5. Additional Uses

The Examiner has provided no evidence that the claimed nucleic acid molecules will not work for the additional disclosed utilities.[6] It appears that the Examiner is arguing that such uses are legally insufficient under 35 U.S.C. §101. This is wrong as a matter of law. The Examiner "has the initial burden of challenging a presumptively correct assertion of utility in the disclosure." *In re Brana*, 51 F.3d 1560, 1567, 34 U.S.P.Q.2d 1436, 1441 (Fed. Cir. 1995). The Examiner "must do more than merely question operability – [he] must set forth factual reasons which would lead one skilled in the art to question the objective truth of the statement of

[6] The Examiner has questioned whether the disclosure is sufficient to practice "antisense" technology. Office Action dated March 22, 2000 at page 13. However, the Examiner has failed to provide any evidence supporting his position.

operability." *In re Gaubert*, 524 F.2d 1222, 1225-26, 187 U.S.P.Q. 664, 666 (C.C.P.A. 1975) (emphasis in original). The Examiner has not met this burden.

The additional disclosed uses are directly analogous to the uses of a microscope or a cell based assay (*see* Section 1.b., *supra*). The claimed nucleic acid molecules can be introduced into a plant or plant cell (either as sense molecules or antisense inhibitors), which can then be used, similar to a cell based assay, to screen for compounds, such as a herbicide. For example, a compound can be provided to both an "antisense plant" and a control plant (no antisense) and the effect of the compound on the plant can be monitored. Such a screen is analogous to the cell-based assay described in Section 1.b., which has a legally sufficient utility. Thus, the use of a plant or plant cell having an introduced claimed nucleic acid molecule is a legally sufficient utility. Moreover, the claimed nucleic acid molecules have a variety of additional uses such as identifying and isolating proteins that bind to the claimed nucleic acid molecules and the isolation and characterization of the corresponding mRNA, gene and protein.

Indeed, using the claimed nucleic acid molecules to identify and isolate proteins that bind to the claimed nucleic acid molecules and to isolate and characterize the corresponding mRNA, gene and protein is analogous to using a microscope to locate and characterize a plant feature such as a cell type. Thus, the use of the claimed nucleic acid molecules to identify and isolate proteins that bind to the claimed nucleic acid molecules and to isolate and characterize the corresponding mRNA, gene and protein is a legally sufficient utility.

For the reasons above, the premise of the rejection under 35 U.S.C. §101 is incorrect and the rejection should be withdrawn.

2. THE ENABLEMENT REQUIREMENT FOR THE CLAIMED INVENTION HAS BEEN MET

The Examiner has rejected claims 1 and 3 for failing to provide an enabling disclosure for how to use the claimed nucleic acid molecules as a hybridization probe or amplification primer. Because this assertion is made only in reference to the use of the claimed nucleic acid molecules

as a probe or primer, it has no bearing on the other stated utilities in the specification and should therefore be withdrawn as a basis for rejection.

In any event, the assertion is wrongly predicated on the allegation that before the claimed nucleic acid molecules would act as a probe or primer in a hybridization or amplification reaction, one skilled in the art would have to "make-and-test" a myriad of nucleic acid molecules comprising the core sequence. But that is wrong inasmuch as the skilled artisan would be guided by his knowledge of the art in view of the particular purpose for which the claimed nucleic acid molecules were being used.

The parameters of hybridization and the polymerase chain reaction are sufficiently understood so that a person of ordinary skill in the art can readily combine the recited nucleic acid sequence with other nucleic acid sequences and use those nucleic acid molecules. Wiegand Decl. at paras. 9, 13. Such a person could readily determine when the addition of certain sequences such as a polylinker or a bacterial plasmid sequence, such as pSport sequence, to the recited sequence would affect the use of the claimed nucleic acid molecules, for example, as a molecular marker. Wiegand Decl. at para. 13. Moreover, a person of ordinary skill in the art would know that the addition of other soybean sequences (*e.g.*, other soybean ESTs) would, in all likelihood, prevent the efficient use of that combined sequence as a hybridization probe. Wiegand Decl. at para. 13.

Applicants' previously presented an *In re Wands,* 858 F.2d 731, 8 U.S.P.Q.2d 1400 (Fed. Cir. 1988) analysis focused on what Applicants believed to be the Examiner's concern – namely that one skilled in the art would not know how such molecules could be made. However, the Examiner concedes that "[o]ne skilled in the art would know how such molecules could be made". Office Action dated March 22, 2000 at page 18. Instead, the Examiner asserts that the "specification fails to provide an enabling disclosure for how to use the claimed nucleic acid molecules as hybridization probe or amplification primer that is commensurate in scope with the

claimed nucleic acid molecules." Office Action dated March 22, 2000 at page 18. But, a reasonable analysis of the *In re Wands* criteria also leads to the conclusion that the claimed invention would not require undue experimentation to make and use nucleic acid molecules that combine the recited nucleic acid sequence with other nucleic acid sequences in the disclosed utilities.

The first *Wands* criterion is the quantity of experimentation necessary. As mentioned above, the "make-and-test" "quantum" of experimentation is reduced by the extensive knowledge, for example of the hybridization parameters, to which a person of ordinary skill in the art has access. *See*, for example, the hybridization parameters set forth in Sambrook *et al.* (eds.), *Molecular Cloning: A Laboratory Manual*, 2d ed., pp. 9.47-11.61, Cold Spring Harbor Laboratory Press, Plainview, New York (1989) and Haymes *et al.*, *Nucleic Acid Hybridization, A Practical Approach*, IRL Press, Washington, DC (1985). Accordingly, the addition of nucleotides to the recited sequence that would not alter the hybridization ability of such nucleic acid molecules is well within the skill of those working in this technology.

The second criterion is the amount of direction or guidance given. The specification provides guidance, for example, on hybridization parameters in the context of the disclosed utilities. Such direction or guidance includes: illustrative hybridization conditions (specification at page 18, lines 8-21); references setting forth methodology that includes the hybridization of nucleic acid molecules to detect polymorphisms (specification at page 29, line 6 - page 35, line 3); references setting forth methodology that includes the hybridization of nucleic acid molecules for *in situ* hybridization (specification at 38, lines 10-23); and references setting forth methodology that includes the hybridization of nucleic acid molecules for microarray analysis (specification at page 40, lines 14-22).

The third criterion is the presence or absence of working examples. The working examples disclose hybridization steps. In particular, the working examples disclose a sequencing

reaction that has a hybridization step where a universal primer hybridizes to a sequence present in pSport immediately 5' to the cDNA insert from which the disclosed sequence was obtained.

The fourth criterion focuses on the nature of the invention. There are a variety of uses that involve a hybridization step for the claimed nucleic acid molecules comprising, consisting essentially of, or consisting of SEQ ID No. 1. Practitioners in this art have available to them considerable knowledge on the conditions and approaches that can be utilized for such a step. Practitioners in this art are also prepared to try multiple methods to obtain the desired result. Wiegand Decl. at paras. 10-11.

The fifth and sixth criteria focus on the state of the art and the relative skill in the art. Methods needed to practice the invention are known in the art as well as procedures to carry out the hybridization steps. *See*, for example, Sambrook *et al., Molecular Cloning: A Laboratory Manual,* Cold Spring Harbor (1989), Mailga *et al., Methods in Plant Molecular Biology,* Cold Spring Harbor (1995) and Birren *et al., Genome Analysis: Analyzing DNA,* 1, Cold Spring Harbor (1997) and Haymes *et al., Nucleic Acid Hybridization, A Practical Approach*, IRL Press, Washington, DC (1985. These references are available to guide use of the claimed nucleic acid molecules. It is clear from these resources, and particularly the guidance given on how to carry out the hybridization step, that a person of ordinary skill in the art would be able to use the claimed nucleic acid molecules for the disclosed utilities.

The seventh criterion considers the predictability of the art. The art to be considered here is the art associated with modifying nucleic acid molecules and the use of the modified nucleic acid molecules. The above analysis reveals that the parameters of a hybridization step are sufficiently predictable and that a person of ordinary skill in the art can advantageously rely upon this predictability when undertaking the disclosed utilities with the claimed nucleic acid molecules.

The eighth criterion focuses on the breadth of the claims. Enablement is satisfied when the disclosure "adequately guide[s] the art worker to determine, without undue experimentation, which species among all those encompassed by the claimed genus possess the disclosed utility". *See In re Vaeck,* 947 F.2d 488, 496, 20 U.S.P.Q.2d 1438, 1445 (Fed. Cir. 1991). Here, enablement is satisfied because the art worker is guided by the disclosure to look, for example, to known hybridization parameters in making that determination.

The Examiner asserts a number of shortcomings with respect to Applicants' prior *In re Wands* analysis. Office Action dated March 22, 2000 at page 18, line 13 - page 20, line 12. In essence, these alleged shortcomings can be summarized as whether the level of skill in the art and state of the prior art would enable one skilled in the art to predict, *a priori,* with a reasonable degree of certainty, the molecules capable of being used in one of the disclosed utilities. To the extent that the Examiner contends that there is a requirement for a precise *a priori* predictability without recourse to any experimentation, that position is without legal support. *Cf. Atlas Powder Co. v. E. I. du Pont de Nemours & Co.*, 750 F.2d 1569, 1576, 224 U.S.P.Q. 409, 413 (Fed. Cir. 1984) ("[t]hat some experimentation is necessary does not preclude enablement"). And here, for reasons demonstrated above, sufficient predictability with a reasonable degree of certainty **is** present, taking into account routine experimentation. Accordingly, the premise of the rejection is incorrect and it should be withdrawn.

3. THE CLAIMS SATISFY THE WRITTEN DESCRIPTION REQUIREMENT

The Examiner rejects claims 1 and 3 based on the assertion that a failure to specifically describe substantial species within the claims (particularly the full length mRNA, cDNA and genomic sequences) constitutes a failure to satisfy the written description requirement for the claims. However, the Examiner recognizes that the specification does disclose SEQ ID No: 1 and generically vectors containing such sequences.

The Examiner is wrong as a matter of law in concluding that the nucleic acid sequence disclosed as SEQ ID No: 1 fails to provide a satisfactory written description of claims 1 and 3. As already set forth in Applicants' Response dated July 6, 1999, if a person of ordinary skill in the art would have understood the inventor to have had possession of the claimed invention, even if not every nuance, then the written description requirement is met. *In re Alton*, 76 F.3d 1168, 1175, 37 U.S.P.Q.2d 1578, 1584 (Fed. Cir. 1996). An applicant is not required to "describe" all things that are encompassed by the claims in order to satisfy 35 U.S.C. § 112. Applicants have here provided the sequence of the claimed nucleic acid molecules and thus have established possession of the claimed invention. The fact that the claims at issue are intended to cover molecules that include the recited sequences joined with additional sequences does not mean that Applicants were any less in possession of the claimed nucleic acid molecules.

The Examiner asserts that because the claims cover full length mRNAs, cDNAs and genomic sequences that include SEQ ID No: 1, a failure to specifically describe the full length nucleic acid molecules result in the claims lacking written description. In short, the Examiner's view is that an applicant must first characterize the mRNA, cDNA, genomic DNA, intron, regulatory region or promoter region, before being accorded credit for possession of the recited sequence. Even if such characterization were required if the claim specifically did call for the full-length nucleic acid molecules, it is not required when the only claim requirement is the recited sequence.[7] Furthermore, even without a particularized disclosure of a full-length sequence such as an mRNA, cDNA, genomic region, regulatory region or a promoter region, Applicants have sufficiently described the claimed nucleic acid molecules such that they may be used to practice the disclosed utilities. Thus, Applicants had possession of the claimed invention by their disclosure of SEQ ID No. 1. Nothing else is necessary.

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[7] The fact that more than the recited sequence can be present without escaping the claim coverage does not change the fact that only the recited sequence is *required* by the claims.

The Examiner further asserts that "in the absence of any information regarding the basic and novel characteristics of the claimed invention, recitation of 'consisting essentially of' in claim 3 fails to distinguish the invention of claim 3 from that of claim 1, which recites 'comprising.'" Office Action dated March 22, 2000 at page 22, lines 10-14. However, the Examiner is in error in stating that Applicants failed to disclose any basic and novel characteristic of the claimed invention. Certain of the above-disclosed utilities (*see* Sections c.1-5, *supra*) require the claimed nucleic acid molecules to hybridize to naturally occurring nucleic acid molecules. The ability to hybridize to such a molecule is clearly a basic and novel characteristic of the claimed invention. The term "consisting essentially of" is one that excludes ingredients that may materially affect a basic and novel characteristic of the claimed composition – here the ability to hybridize to naturally occurring nucleic acid molecules. Accordingly, the premise of the rejection is incorrect and it should be withdrawn.

4. THE CLAIMS ARE NOT INDEFINITE

The Examiner has rejected claim 1-3 as being indefinite in using the term isolated. The definition of the term "substantially purified" is irrelevant to the metes and bounds of the term "isolated" as this definition is not the definition of the term isolated and is not relied upon for support of the term isolated. Moreover, when properly read in context the term "isolated" refers to isolated from other nucleic acid molecules. Consequently the metes and bounds of the term isolated were indeed clear. Nonetheless, to expedite prosecution Applicants have amended claims 1 and 3 to recite the phrase "isolated from other nucleic acid molecules." This amendment is supported, for example, at page 68, lines 1-6. Claim 2 has been amended to remove the term "isolated" from the claim.

5. THE REJECTION UNDER 35 U.S.C. §102(B) IS OVERCOME BY AN APPROPRIATE READING OF THE TERM "ISOLATED"

Claims 1 and 3 were rejected under 35 U.S.C. §102(b) as being anticipated by Reams. The premise of the rejection was that a reasonable interpretation of the term isolated embraces a total nucleic acid preparation. We disagree. However, for the reasons set forth in the preceding section 4, it is respectfully submitted that the anticipation rejection is obviated by the proposed amendment and should be withdrawn.

Respectfully submitted,

Date: August 22, 2000

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